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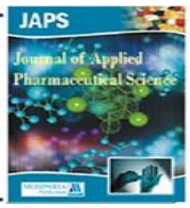

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Cubic Spline and Determination of Changes in the Solid Dispersion of Cefuroxime Axetil by Using MATLAB Software

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ABSTRACT

Studies in pharmaceutical systems are used to pick up the physicochemical properties of drugs, one of them are solid dispersions requiring a carrier to achieve that purpose. Generally hydrophilic agents are used as a carrier, because they have high hydrophilicity and are used in the pharmaceutical industry as excipients. In this work the Urea merges with Cefuroxime Axetil (CFA) for the formation of three solid dispersions, the antibacterial drug (CFA) is insoluble in water, creating problems of bioavailability in the body. Solid Dispersion of CFA was prepared with a ratio of 1:1, 1:2 and 1:3 using Urea. The study of bioactivity of the solid solutions was performed by Differential Scanning Calorimetry (DSC) and showing that part of CFA is retained in the volume (structure) of Urea and some joins the surface. The data analyzed were for the absorbance of each sample that were applied a cubic interpolation to determine differences between the dispersions by using MATLAB software (V.No. R201 1b).

Keywords: CFA, data matrix, Urea, solid dispersions, Cubic Slpine, AUC, MATLAB.

INTRODUCTION

Studies in pharmaceutical systems where altering the properties of the drugs when they have problems with solubility (Herbert A *et al.*, 2000), gastric irrigation or even fraction of the dose administered to the patient (Kafia M. *et al.*, 2009). In the most common mentioned are drug encapsulation, use of porous matrices and the development of solid dispersions, where chemical dealing polymeric substances such as cyclodextrins, hydroxy methylcellulose (HPMC) and cellulose derivatives (Urea, Albumin) and polyethylene glycols (PEGs) in the pharmaceutical industry have many uses (D. K. Sharma *et al.*, 2007) Because of the variation which presents the molecular weight of these polymers are used as excipients, such as low molecular weight PEGs (400-200), used in liquid formulations, eye drops, presentations and fillings parenteral gelatine capsules, as bases in the manufacture of ointments and suppositories or as active ingredients in the manufacture of ophthalmic demulcent. 3350PEGs are used in laxatives and those with molecular weights greater than 20000 Daltons are used in organ preservation (M. Franco *et al.*, 2001).

Cefuroxime Axetil (CFA) is a Cephalosporin-derived drug which is broad spectrum antibacterial but it has poor water solubility in water (S. C. Arora et al., July-Sep 2010).Therefore, in this research are to improve the water solubility and dissolution rate of CFA using Urea as a carrier using the technique of solid dispersions by varying the concentration of Urea with respect to CFA, getting three solid dispersions: CFA: Urea (1:1), CFA: Urea (1:2) and CFA : Urea (1:3) which as mentioned are the study samples. Then apply a cubic interpolation to each of the samples only for the absorbance of each of the solid dispersions of CFA and obtain values that are not tabulated.

Uses of Cubic Slpine

In mathematical and experimental models this behaviour can be measured with an interpolation and polynomial approach. The analysis performed by the absorbance data obtained, this will be done by interpolation, which consist to find a figure within a range in which extreme values are known. The general problem of interpolation is when you have a function which is only known by a number of points in the same and when you want to find the value of a halfway point of the function, a function whose graph passes through these points is necessary to estimate the desired values. The interpolation used for this work was the cubic spline (Corina Maria Dinis et al., 2009). The cubic splines are used to compare the curves obtained for each sample of the absorbance of the solid dispersion of CFA, and later to determine differences between them using the area under the curve of each spline and to conclude whether the differences are significant for that experiment (R. L. Burden and D. Faires et al., 1992)

MATERIAL AND METHOD

Material

CFA is obtained as gift sample from orchid chemicals Hyderabad. And the other chemicals are of obtained from Rankem, Mumbai**.**

Method

Three solid dispersions were obtained of CFA and Urea with varying the concentration of urea compared to CFA in the following way: for 100 gram of was added in a platinum crucible 100, 200 and 300 g of Urea (in different events), the homogeneous solid mixture melts at 80 º C for 5 minutes and then allowed to cool to room temperature. (Figure1)

RESULT AND DISSCUSSION

DSC Analysis

The thermograms of CFA-Urea solid dispersions show (Figure2) a single endothermic peak, corresponding to the polymer without registering the thermal effects due to the drug. This is attributed to the liquid state where there is a miscibility between both compounds and has been able to form a eutectic mixture which indicates that CFA may be occluded in the bulk of Urea and not on the surface of it, because no bands of diffraction characteristics of CFA in the solid dispersions are observed. This follows because the homogeneous solid mixtures that melt at 85^0 C lower than the melting point has CFA, so it is still in solid dispersions, as confirmed by DSC studies.

Determination of AUC

The first phase consisted of calculating the absorbance values for each stage of solid dispersion in 1:1, 1:2, 1:3 and marketed preparation (Naxim 250) (Table 1).

Table.1: Absorbance values for each stage of solid dispersion in 1:1, 1:2, 1:3 and marketed preparation.

Sr. No.	Time (Min)	1:1	1:2	1:3	Marketed
1	0	0	0	0	0
2	20	0.069	0.078	0.537	0.324
3	40	0.084	0.090	0.867	0.667
4	60	0.106	0.114	0.911	0.789
5	80	0.119	0.146	1.002	0.898
6	100	0.126	0.171	1.101	0.991
7	120	0.147	0.181	1.128	1.042

The following program calculates the cubic spline for the absorbance of each solid dispersion of CFA, which was programmed using MATLAB software, which shows the calculation of cubic spline for the sample of prepared solid dispersion.

y = [0, 0.0690 0.0840 0.1060 0.1190 0.1260 0.1470]
x = [0, 20 40 60 80 100 120]
Absorbance of the solid dispersion of CFA is plotted to a 1:1
Plot (x,y,r)
Spline function is calculated
pp = spline(x,y)
7 values not tabulated are evaluated
z = linespace(0, 120, 7) spline function is evaluated for these values
sval = ppval (pp, z)
spline function is plotted with these values
Plot (z, sval, and 'b')
The area of the spline is calculated of solid dispersion
Area I = trapz (x, y)
Area II = trapz (z, sval)
Area I = 11.6500
Area I = 11.6500
Where:

X is the data for the X axis
Z is the vector with values not tabulated, (100).
Y is the values for Y axis
pp is the values of the Spline values not tabulated Sval are the values of the spline function
Area I = area under the curve of the sample
Area II = area under the curve of the Spline.

Similarly, the cubic spline for each solid dispersion of CFA, which was programmed using MATLAB, is calculated and the results are filled in table 2. Once obtained the splines of each sample, we calculated the area under the curve of each spline, using the method of trapezoids (The method involves dividing the curve by a series of vertical lines into a number of trapezoids, calculating separately the area of each trapezoid and adding them together).

$$AUC = \frac{t2-t1(c1+c2)}{2}$$

Where,

t_1 = final time

t_2=Initial time

C_1=con^c. at time t_1

C_2=con^c. at time t_2

The results of AUC by trapezoidal rule and obtained with the spline. With the data the percentage relative error was calculated which was committed to determine differences that may have these areas of the splines (Table2).

Table. 2: Area under the curve of sample and spline.

Sr. No.	Ratio	AUC Sample (by trapezoid's rule)	AUC spline
1	1:1	11.65	11.5500
2	1:2	13.80	13.7300
3	1:3	99.61	99.600
4	Marketed	93.83	93.7800

Determination of percent relative error

It is notorious that the differences between the areas of the Spline and samples is not significant, the differences are not large, but it is also significant that the areas are different for the samples and the Spline, so we can say that in form are different. To determine the relative error percentage of the samples and the Spline function takes the area of the sample and is subtracted Spline area divided by the sample area multiplied by 100.

$$\% \text{ relative error} = \frac{\text{AUC of sample} - \text{AUC spline}}{\text{Sample Area}} \times 100$$

Table. 3: Relative percentage errors between sample and spline for each ratio.

% relative error for1:1	% relative error for1:2	% relative error for1:3	% relative error for marketed preparation
0.8583	0.5070	0.0100	0.0534

The smallest % relative error is observed in solid dispersion was 1:3 so you can say it is the sample with a softer Spline denoting a higher dissolution rate with respect to the other samples (Table3). Graphical Splines while the absorbance of the solid dispersion of CFA taking as range of 20 to 120 minutes predicted points were not assessed in the samples is well known that the differences between the spline and the samples obtained are significant. (Graph I, II, III).

We can say that the graphics are significantly different even though it is the same variable that measures the absorbance, but undoubtedly the best performance is shown in graph III, which refers to the solid solution of CFA to 1:3, as which is softer and therefore conclude that it is the one that has better dissolution rate, a situation that coincides with the physicochemical analysis performed.

Comparative dissolution profile of marketed and tablet prepared tablet

The dissolution profile of tablet prepared by solid dispersions compared with commercial tablets and the results were between 20 and 60% drug release over the business from the standpoint of physical chemistry. It should be mentioned that the force of compression used, gives the appropriate hardness to ensure dissolution of the drug. The results of Figure 1 indicate that the solid dispersion dissolution rate was better was the CFA-Urea1:3 which are much more than commercial tablets of CFA (Figure 2)

Fig. 1: Photograph of prepared Solid Dispersion.

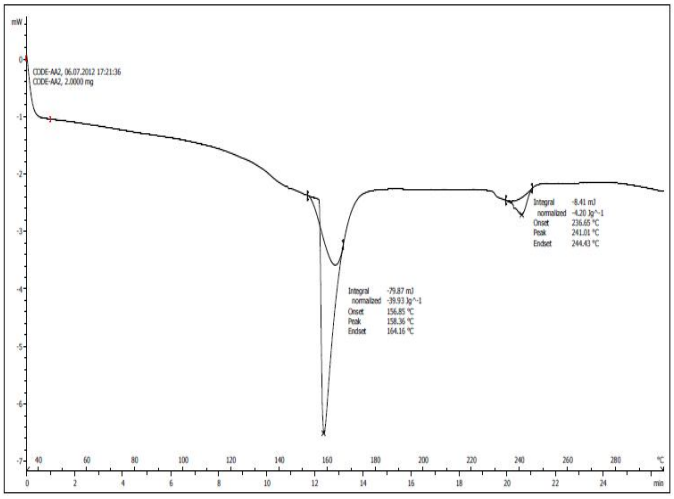


Fig. 2: The thermograms of CFA-Urea solid dispersions.

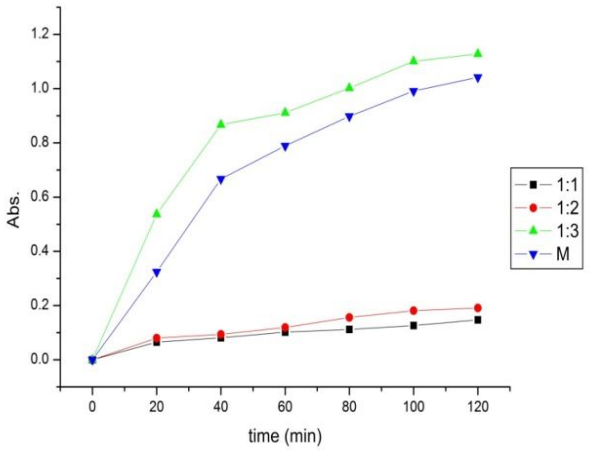
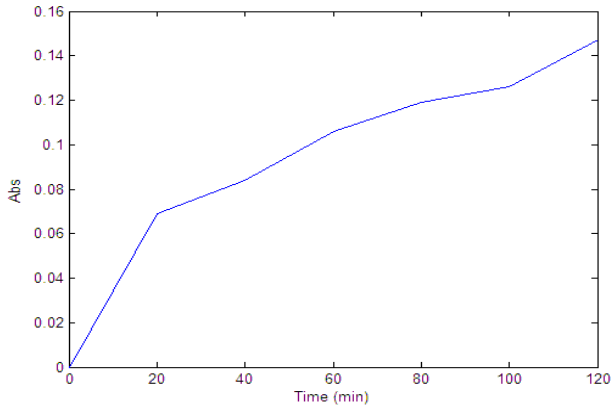
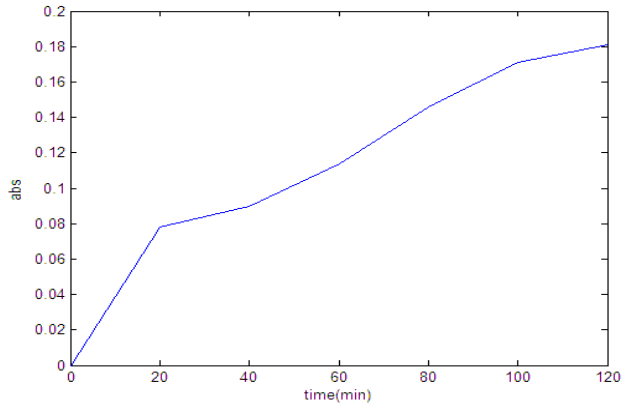


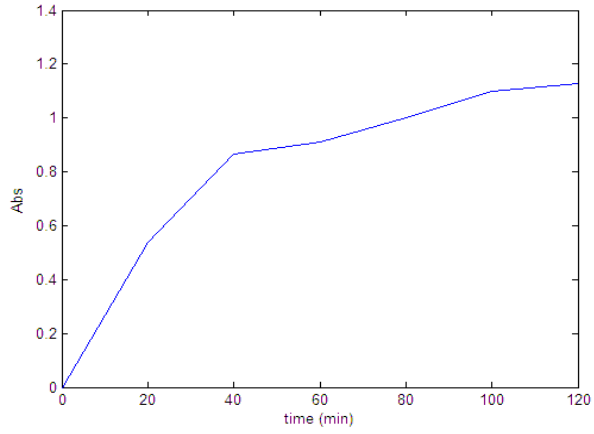
Fig 3. Release of CFA, compared with solid dispersions commercial CFA.



Graph 1. Cubic Spline for the sample to 1:1



Graph 2. Cubic Spline for the sample to 1:2



Graph 3. Cubic Spline for the sample to 1:3

CONCLUSIONS

Cubic interpolation allow the segmentation of the samples of the experiment to improve the dissolution of CFA, consisting of three stages, allowing both numerically and graphically demonstrate that there are changes in the dissolution of CFA, where it is evident that the best solution was the solid dispersion of CFA 1:3 against commercial.

FUTURE PROSPECTIVES

The results are satisfactory and continue working on this technique for future analysis, as do cubic interpolation not only to a column of data but for more variables to enrich the analysis. The mathematical software's like METLAB can satisfactory used in formulation and development of pharmaceutical products. It can also be used to determine the significant changes in formulation with respect to time.

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